

CLAIMS

We claim:

1. An isolated, pure population of mammalian CNS
glial restricted precursor cells that is capable of
5 generating oligodendrocytes and at least two distinct
populations of astrocytes.

2. The population of claim 1 wherein said glial
restricted precursor cells are isolated from a mammal
selected from the group consisting of human and non-human
10 primates, equines, canines, felines, bovines, porcines,
ovines, and lagomorphs.

3. The population of claim 1 wherein said glial
restricted precursor cells express cell surface antigens
recognized by the A2B5 monoclonal antibody, but do not
15 express embryonic neural cell adhesion molecule.

4. The population of claim 1 wherein said glial
restricted precursor cells acquire the ability to respond
to platelet-derived growth factor as a mitogen after growth
in vitro in the presence of medium containing fibroblast
20 growth factor and platelet-derived growth factor.

5. The population of claim 1 wherein said glial restricted precursor cells are capable of differentiating into oligodendrocytes, A2B5-positive process-bearing astrocytes, and A2B5-negative astrocytes with fibroblast-like morphology.

6. The population of claim 1 wherein said glial restricted precursor cells are capable of self renewal in adherent feeder-cell-independent culture medium and of differentiation to CNS glial cells but not to CNS neuronal cells.

7. A method of isolating a pure population of mammalian CNS glial restricted precursor cells comprising the steps of:

(a) removing a sample of CNS tissue from a mammal at a stage of development after closure of the neural tube;

(b) dissociating cells comprising the sample of CNS tissue removed from the mammal; and

(c) purifying from the dissociated cells a subpopulation expressing a selected antigen defining glial restricted precursor cells.

8. The method of claim 7 wherein said selected antigen defining glial restricted precursor cells is a cell surface antigen recognized by the A2B5 antibody.

9. The method of claim 7 wherein said purifying
5 comprises a procedure selected from the group consisting of specific antibody capture, fluorescence activated cell sorting, and magnetic bead capture.

10. The method of claim 9 wherein said procedure is specific antibody capture.

10 11. The method of claim 7 wherein said mammal is selected from the group consisting of human and non-human primates, equines, canines, felines, bovines, porcines, ovines, and lagomorphs.

12. A pure population of mammalian CNS glial
15 restricted precursor cells isolated by the method of claim 7.

13. A method of obtaining glial cells comprising:
(a) providing glial restricted precursor cells; and
(b) plating the glial restricted precursor cells
20 under differentiating conditions, thereby causing the glial

restricted precursor cells to differentiate into glial cells.

14. The method of claim 13 wherein said differentiating conditions comprise addition to growth medium of an effective amount of a factor that promotes differentiation into non-process bearing A2B5⁻GFAP⁺ astrocytes and said glial cells are A2B5⁻GFAP⁺ astrocytes.

15. The method of claim 14 wherein said factor that promotes differentiation into non-process bearing A2B5⁻GFAP⁺ astrocytes comprises fetal calf serum.

16. The method of claim 13 wherein said differentiating conditions comprise addition to growth medium of an effective amount of a factor that promotes differentiation into process bearing A2B5⁺GFAP⁺ astrocytes and said glial cells are A2B5⁺GFAP⁺ astrocytes.

17. The method of claim 16 wherein said factor that promotes differentiation into process bearing A2B5⁺GFAP⁺ astrocytes comprises ciliary neurotrophic factor and basic fibroblast growth factor.

18. The method of claim 13 wherein said
differentiating conditions comprise addition to growth
medium of an effective amount of a factor that promotes
differentiation into oligodendrocytes and said glial cells
5 are oligodendrocytes.

19. The method of claim 18 wherein said factor that
promotes differentiation into oligodendrocytes comprises
platelet-derived growth factor and thyroid hormone (T3).

20. A method for treating a neurological or
10 neurodegenerative disease comprising administering to a
mammal in need of such treatment an effective amount of
glial restricted precursor cells or derivatives thereof or
mixtures thereof.

21. The method of claim 20 wherein said glial
15 restricted precursor cells or derivatives thereof or
mixtures thereof are caused to proliferate and
differentiate *in vitro* prior to being administered.

22. The method of claim 20 wherein said glial
restricted precursor cells or derivatives thereof or
20 mixtures thereof are caused to proliferate *in vitro* prior
to being administered, and then are caused to further

proliferate and differentiate *in vivo* after being administered.

23. The method of claim 20 wherein said glial restricted precursor cells or derivatives thereof or
5 mixtures thereof are caused to proliferate *in vitro* prior to being administered, and then are caused to differentiate *in vivo* after being administered.

24. The method of claim 20 wherein said glial restricted precursor cells or derivatives thereof or
10 mixtures thereof are from a heterologous donor.

25. The method of claim 24 wherein said donor is a fetus.

26. The method of claim 24 wherein said donor is a juvenile.

15 27. The method of claim 24 wherein said donor is an adult.

28. The method of claim 20 wherein said glial restricted precursor cells or derivatives thereof or mixtures thereof are from an autologous donor.

29. The method of claim 28 wherein said donor is a fetus.

30. The method of claim 28 wherein said donor is a juvenile.

5 31. The method of claim 28 wherein said donor is an adult.

32. The method of claim 20 wherein said disease is selected from the group consisting of multiple sclerosis, spinal cord injury, CNS trauma, conditions in which axonal
10 regeneration are desired, conditions in which control or reduction in glial scarring are desired, any dysmyelinating disorder, or an enzymatic disorder.

33. The method of claim 20 wherein said glial restricted precursor cells or derivatives thereof or
15 mixtures thereof are administered locally in the CNS.

34. The method of claim 20 wherein said glial restricted precursor cells or derivatives thereof or mixtures thereof are widely administered in the CNS.

35. The method of claim 20 wherein said glial restricted precursor cells or derivatives thereof or mixtures thereof are administered in an encapsulation device.

5 36. The method of claim 20 wherein said derivatives thereof are obtained by differentiation of glial restricted precursor cells *in vitro*.

10 37. The method of claim 20 wherein said derivatives thereof are obtained by genetic transduction of glial restricted precursor cells.

38. A method for treating neurodegenerative symptoms in a mammal comprising the steps of:

- (a) providing a pure population of glial restricted precursor cells;
- 15 (b) genetically transforming said glial restricted precursor cells with a gene encoding a growth factor, neurotransmitter, neurotransmitter synthesizing enzyme, neuropeptide, neuropeptide synthesizing enzyme, or substance that provides protection against free-radical
- 20 mediated damage thereby resulting in a transformed population of glial restricted precursor cells that express said growth factor, neurotransmitter, neurotransmitter

synthesizing enzyme, neuropeptide, neuropeptide
synthesizing enzyme, or substance that provides protection
against free-radical mediated damage; and

(c) administering an effective amount of said
5 transformed population of glial restricted precursor cells
to said mammal.

39. A method of using glial restricted precursor
cells for reducing glial scar formation associated with
surgical procedures at a lesion site in the central nervous
10 system comprising the steps of:

(a) providing a composition comprising cells
selected from the group consisting of a purified population
of glial restricted precursor cells, derivatives thereof,
and mixtures thereof;

15 (b) administering said an effective amount of said
composition into and adjacent to said lesion site within
two weeks following traumatic injury thereto.

40. The method of claim 38 wherein said composition
comprises encapsulated cells.

20 41. The method of claim 38 wherein said composition
further comprises O-2A progenitor cells.

42. A method for promoting wound healing at a lesion site in the central nervous system comprising the steps of:

(a) providing a composition comprising cells selected from the group consisting of a purified population of glial restricted precursor cells, derivatives thereof, and mixtures thereof;

(b) administering an effective amount of said composition into and adjacent to said lesion site within two weeks following traumatic injury thereto.

43. A method for promoting neuronal survival or axonal regeneration or both in the central nervous system comprising the steps of:

(a) providing a pure population of glial restricted precursor cells or derivatives thereof or mixtures thereof;

(b) administering an effective amount of the population of glial restricted precursor cells or derivatives thereof or mixtures thereof to the CNS of the mammal into regions of neuronal injury or regions in which axonal regeneration is required.

44. A method for treating neurodegenerative symptoms in a mammal comprising the steps of:

(a) providing a pure population of glial restricted

precursor cells or derivatives thereof of mixtures thereof;

(b) administering an effective amount of the population of glial restricted precursor cells or derivatives thereof or mixtures thereof to the CNS of the
5 mammal.

45. A method for treating neurodegenerative symptoms in a mammal comprising the steps of

(a) providing a pure population of glial restricted precursor cells or derivatives thereof or mixtures thereof;

10 (b) placing the glial restricted precursor cells or derivatives thereof or mixtures thereof in an encapsulation device to result in encapsulated cells; and

(c) administering an effective amount of the encapsulated cells to the CNS of the mammal.

15 46. A method for treating neurodegenerative symptoms in a mammal comprising the steps of:

(a) providing a pure population of glial restricted precursor cells or derivatives thereof or mixtures thereof;

20 (b) placing the glial restricted precursor cells or derivatives thereof or mixtures thereof on or in a scaffold to result in scaffold-associated cells; and

(c) administering an effective amount of the population of scaffold-associated cells to the CNS of the mammal.

47. A method for promoting axonal growth along
5 defined scaffolds comprising the steps of:

(a) providing a pure population of glial restricted precursor cells or derivatives thereof or mixtures thereof;

(b) implanting a scaffold such that a bridge is formed between a region where a desired population of
10 neurons exists and a region to which neuronal growth is desired; and

(c) placing an effective amount of the glial restricted precursor cells or derivatives thereof or mixtures thereof on or in the scaffold.

15 48. A method for screening compounds for neurological activity comprising the steps of:

(a) providing a pure population of glial restricted precursor cells or derivatives thereof or mixtures thereof cultured *in vitro*;

20 (b) exposing said cells or derivatives thereof or mixtures thereof to a selected compound at varying dosages; and

(c) monitoring the reaction of said cells or derivatives thereof or mixtures thereof to said selected compound for selected time periods.

49. A method for continuously propagating glial
5 restricted precursor cells comprising the steps of:

(a) providing said glial restricted precursor cells;
and

(b) culturing said glial restricted precursor cells
in vitro in the presence of minimal essential salts and
10 effective amounts of platelet derived growth factor and
fibroblast growth factor.